REMARKS

This is in response to the Official Action of July 7, 2004. The points raised therein are addressed below in the order originally set forth.

Newly presented claims 52-58 are directed to preferred embodiments of the invention and are added to complete the record.

Newly presented claim 52 comprises in combination the features previously set forth in claims 1, 3, 5, 12, and 21. Thus new claim 52 constitutes present claim 1 with the following additions and deletions:

> 52 (newly presented). A chemical construct for use in solid phase synthesis comprising:
>
> a solid support Q having linked thereto via a connecting group Y a substrate R;
>
> the connecting group Y having first and second cleavage sites which are orthogonally and selectively cleavable;
>
> the second cleavage site being selectively cleavable to release the substrate; and the first cleavage site being located at a position between the second cleavage site and the solid support and being selectively cleavable to release a fragment Fr comprising the substrate and at least a portion of the connecting group Y;
>
> and a moiety comprising a basic amino sensitising group G in masked form ~~on the chemical fragment Fr~~ at the first cleavage site wherein the chemical fragment Fr contains a ~~means~~ peak splitting isotopic label located between the first and second cleavage sites for imparting a characteristic signature to the mass spectrum of the fragment;
>
> wherein the first cleavage site is selectively cleavable by one type of chemistry selected from a group of chemistries consisting of cleavage under acid conditions, base catalysed cleavage, oxidative cleavage, reductive cleavage, nucleophilic displacement, cleavage by 1,2 *bis* nucleophiles, electrophilic displacement, and thermal, photochemical and enzymatic cleavage, and the second cleavage site is selectively cleavable by a different type of chemistry selected from the said group.

Newly presented claim 53 corresponds to previously presented claim 4, except it is dependent upon claim 52.

Newly presented claim 54 corresponds to previously presented claim 13, except it is dependent upon claim 53.

Newly presented claim 55 corresponds to previously presented claim 22, except it is dependent upon claim 54.

Newly presented claim 56 corresponds to previously presented claim 23, except that it is dependent upon claim 55.

Newly presented claim 57 corresponds to previously presented claim 27, except that it is dependent upon claim 56.

Newly presented claim 58 recites the Rink linker feature previously deleted from (but originally presented in) claim 27.

Claims 1, 3-6, 10, 12, 13, 17-23 and 27 stand rejected under 35 USC 112, first paragraph, as lacking written description. This rejection is respectfully traversed. The claimed subject matter is directed to combinations of elements in a new and nonobvious manner. Numerous examples of each element were known to those of ordinary skill in the art at the time the application was filed. In such a case, functional or partially functional description of a group has long been approved. *See, e.g.,* In re Johnson, 558 F.2d 1008, 194 USPQ 187 (CCPA 1977)(approving claim recitation in claims for a polyether composed of recurring units, with one unit having electron withdrawing groups substituted thereon, the electron withdrawing groups having a sigma value "sufficient to activate a halogen atom"). As set forth in the recent written description guidelines "The absence of definitions or details for well-established terms or procedures should not be the basis of a rejection under 35 USC §112, ¶1, for lack of adequate written description." Federal Register, Vol 66, pg 1105 (Jan. 5, 2001). Accordingly, it is respectfully submitted that this rejection should be withdrawn.

Claims 1, 3-6, 10, 12, 13, 17-23 and 27 stand rejected under 35 USC 112, second paragraph, for various informalities in the claims. These have been corrected above in the manner suggested by the Examiner, and it is respectfully submitted that this rejection may now be withdrawn.

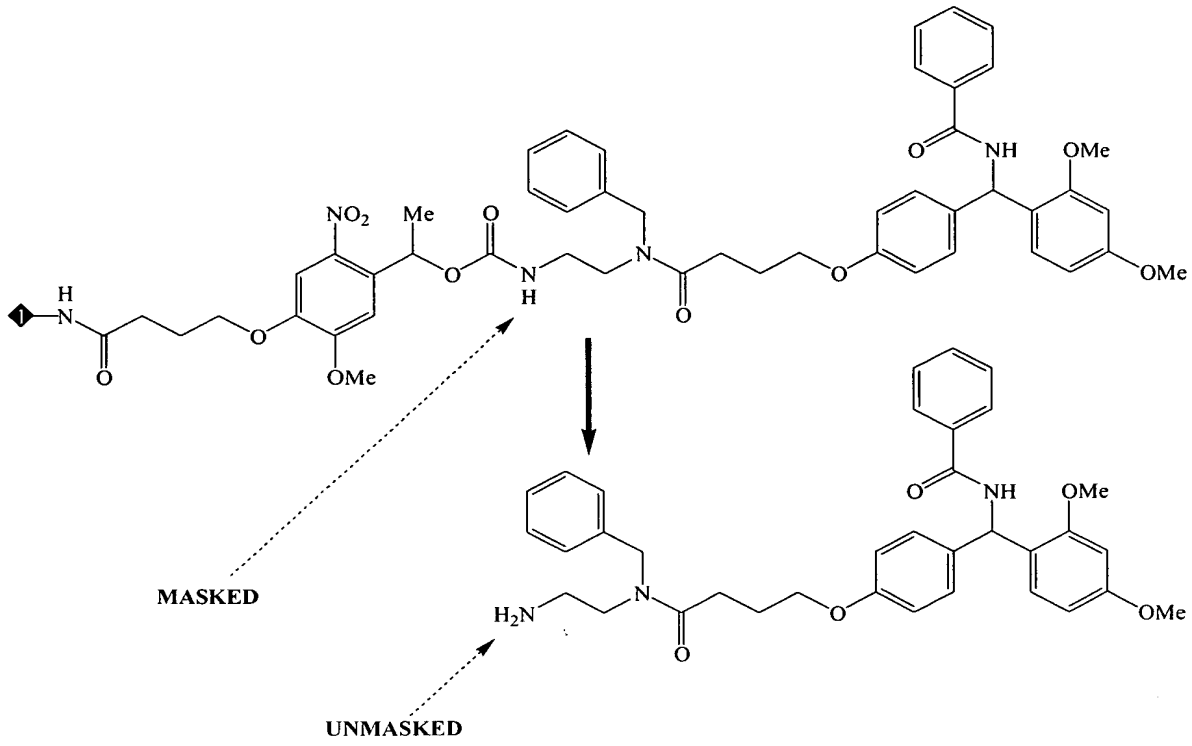
In addition, the remaining claims have been reviewed and other "such as..." phrases removed by amendment above.

Claims 1, 3-6, 10, 12, 13, 17-23 and 27 stand rejected as either anticipated under 35 USC 102(b) or obvious under 35 USC 103 over Carrasco et al. This rejection is respectfully traversed.

As noted in the specification, the sensitising group G is formed or introduced by cleavage of the "skeleton" of the construct. This is in contrast with Carassco et al., where the sensitizing group is present throughout the synthesis of the substrate, or

where the sensitising group is revealed by cleavage of a side chain or removal of a protecting group from a pendant sensitising group (pg 5, lines 20-25). It is stated in the Official Action that, in giving "masked form" its broadest reasonable interpretation, the ionizing tag sequences of Carrasco et al. can be said to be masked, until the desired peptides are cleanly separated away. In the official action, this broadest reasonable interpretation is said to be supported by the specification at page 6, lines 25 to 27, where it is stated that "The atoms or functional group making up the sensitizing group G can be present in a masked form in the construct before cleavage of the fragment F4 from the resin, the cleavage conditions merely serving to unmask the sensitizing group G".

However, it is clear that Carassco teaches an ionization sequence (see scheme 1 therein) that is already ionized (as pointed out in the instant specification at page 4, line 25). **Note particularly the positive charge on the side-chain terminal amino group in the ionization sequence shown in scheme 1 of Carassco.** In contrast, in the chemical construct of the present invention, prior to formation of the fragment by cleavage, the sensitising group G is present "in masked form at the first cleavage site" "before cleavage of the fragment Fr from the resin" (see the specification at page 6, lines 11-12; page 6, lines 25-27). As a tangible example of this difference **note particularly the lack of positive charge on the amine linking group in compound 6, scheme 1, of the instant invention, which is only "unmasked" to a terminal amino group after cleavage** (which terminal amino would bear a positive charge in the present invention). The pertinent portions of this scheme, and the difference noted above, is summarized below:



In the event the prior amendment made unclear that G was masked prior to cleavage, claim 1 is amended above to rephrase "a sensitising group G in masked form *on the chemical fragment Fr* at the first cleavage site" to simply read "a sensitising group G in masked form at the first cleavage site." It is believed the amended language is more consistent with the recitation of the specification.

In view of the foregoing, it is respectfully submitted that the instant invention is neither disclosed nor suggested by Carrasco, and respectfully submitted that this rejection should be withdrawn.

In view of the foregoing, it is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

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